Evaluation of Tl-201 SPECT imaging findings in prostate cancer

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DISCUSSION

Tumor tissues can be screened by radionuclide methods due to some characteristic features such as increased metabolic activity and blood flow, increased vascular permeability and presence of tumor-associated antigens. For imaging of tumors, numerous radiopharmaceutical agents have been developed and introduced into clinical practice.

Tl-201, one of the tumor scanning agent is taken into the cell like potassium (K+) via Na-K ATPase pump. Tl-201 cannot be extracted by non-living cells. In tumor tissues, while increased accumulation of Tl-201 in the extracellular region is thought to be associated with increased vascularity developing due to the formation of new vessels, intracellular accumulation of Tl-201 is mostly related with the viability and metabolic activity of pathological cells (9). Tl-201 uptake was much less in the connective tissues, inflammatory cells and necrotic tissues when it was compared with viable tumor tissues. It was observed that a large portion of the injected Tl-201 dose accumulated in the living tumor tissues (10).

Sehweil et al. found that T/Bg ratios reached the highest level in the early period (first 15-20 minutes) of the study and remained stable for a long time after the injection (11). In this study, imaging and quantification processes were also performed at the first hour when Tl-201 had the maximum activity level.

Correlation between histopathological results, uptake patterns and T/Bg ratios were studied. It has been shown that Tl-201 can be used to determine the effectiveness of diagnosis and treatment in malignant tumors especially brain tumors, breast cancer and soft tissue sarcomas (12, 13, and 14).

In a pilot study which appears as a single example in literature, Yang et al. studied the clinical value of Tl-201 SPECT to differentiate prostate cancer and benign prostate hyperplasia (BPH) in patients with prostate cancer. Unlike the current study, after bioptic diagnosis of prostate cancer (15 patients) and BPH (10 patients) the patients underwent a Tl-201 SPECT imaging on pelvic region The Tl-201 SPECT studies showed tumor uptake in 13/15 (86.7%) patients with prostate cancer but Tl-201 uptake was not observed in any of the 10 patients diagnosed with BPH. The study concluded that Tl-201 SPECT imaging can be used effectively to detect tumor tissues in prostate cancer (15).

Today, imaging techniques are not routinely recommended for the diagnosing and staging of prostate cancer. However, for patients with prostate cancer, independently from the presence of risk factors, 28.6% and 52.4% of clinicians ask for computed tomography and bone scintigraphy tests, respectively (16). In general, in uro-oncological imaging, successful results have been obtained from studies, especially positron emission tomography and scintigraphic imaging with monoclonal antibodies, which have been performed for the detection of tumor tissue and the extent and staging of the disease. The sensitivity and specificity of PET for detecting tumor tissues have been reported as 79% and 66%, respectively (17). PET which is used to distinguish fibrosis and residual tumor tissue occurring after surgery, radiotherapy or chemotherapy can not help to solve this problem completely.

One of the methods used in the evaluation of patients with prostate cancer is SPECT imaging performed with In-111 capromab pendetide (ProstaScint). ProstaScint is generally preferred as a secondary imaging method for patients diagnosed with prostate cancer for the investigation of the extent and the staging of the disease. This imaging modality has 92% sensitivity in detection of prostate cancer metastases (18). It has been reported that ProstaScint has a complementary value independent from PSA level and Gleason score in the evaluation of recurrent or metastatic prostate cancer (19).

PSA is not specific for prostate cancer but it has been reported to be valuable in providing early diagnosis of cancer before the onset of symptoms or detection of DRE findings (20). In the 25% of patients who were diagnosed with prostate cancer by needle biopsy as a result of suspicious findings of DRE, the serum PSA values were less than a 4 ng/dl level (21, 22).

Catalona et al. showed in their studies that the probability of making a diagnosis of prostate adenocarcinoma by needle biopsy was 20% when a PSA level was higher than 2.5 ng/ml and this probability was 50% when PSA

No conflict of interest declared.

value reached over 10 ng/ml (4, 22). In the current study, the PSA values were high (> 10 ng/ml) in 5 patients (13.9%) in the benign group and in 10 patients (43.5%) in the malignant group. In addition, prostate adenocarcinomas were diagnosed in 66.7% of the patients with a PSA value higher than l0 ng/ml.

In patients with a negative biopsy result and elevated PSA level, prostate cancer can be diagnosed in up to 20-23% of these cases when diagnostic biopsies are repeated. (23). According to the current study, re-evaluation by repetition of diagnostic biopsy should be made in the benign group of patients who had Tl-201 uptake if the PSA levels remained high in the follow-up period. Thus, we believe that the diagnostic performance and contribution of Tl-201 SPECT in prostate cancer diagnosis will increase. Before repeating biopsy, which is invasive and annoying to the patients, Tl-201 SPECT results can reduce clinicians worry about the presence of malignity.

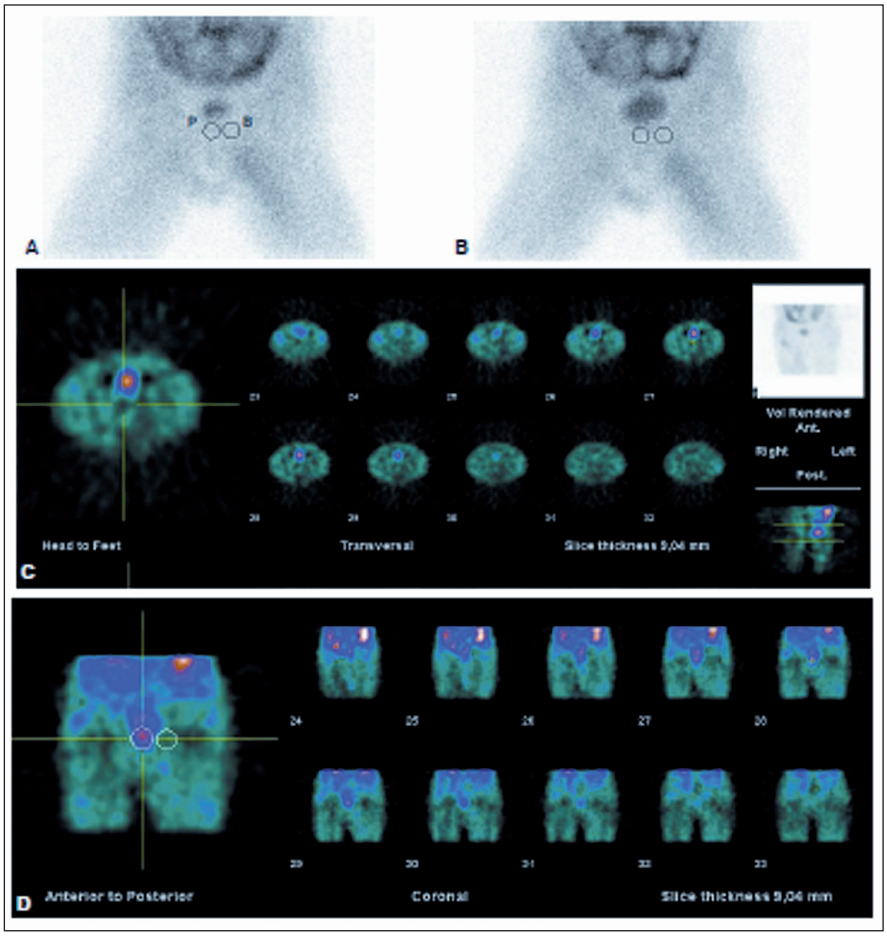
As expected, the T/Bg ratios were significantly higher in patients who had Tl-201 uptake than in patients who had no Tl-201 uptake whether they were in the benign group or the malignant group. While the T/Bg ratio was in the range 1.3 to 0.8 for early, late planar and SPECT images in the benign group, this ratio was found to be higher in the range of 0.9 to 3.2 in the malignant group. However, a cut-off value of T/Bg ratios for the differentiation of benign lesions and malignant lesions was not determined. Some studies have revealed that a 1.5 value was considered a feasible cut-off value between positive and negative manifestations (24, 25). The highest T/Bg ratios were calculated from the patients of the malignant group. In this group, the T/Bg ratio was higher than 1.5 in 13/23 patients. It is believed that this condition may be associated with the better resolution capability of three-dimensional SPECT imaging.

In the current study, ROC analysis was used for the assessment of the T/Bg ratios for planar and SPECT images. The ROC curve is created by the ratio of sensitivity to precision when there is a difference in the level of the cutting in the binary classification systems. The method basically tries to create a balance between accuracy (eliminating capability for false positive results) and sensitivity (the ability to detect true positive results). The size of the area under the ROC curve is directly proportional to the diagnostic accuracy of the test. In this study, areas under the ROC curve were 0.659 ± 0.074, 0.684 ± 0.018 and 0.912 ± 0.041 for the early planar, late planar and SPECT images, respectively. All results were statistically significant ($p < 0.05$). It can be said that SPECT images have a better diagnostic performance to distinguish between malignant and benign cases because the areas under the curve are closer to 1 for the T/Bg ratios of SPECT images. The results of ROC analysis showed that SPECT images had high sensitivity (95.7%), specificity (77.8%), accuracy (84.7%), positive predictive value (73.3) and negative predictive value (96.6%) to discriminate between the malignant and benign groups.

In the current study, the relationship between the Gleason scores with uptake patterns and T/Bg ratios of the patients was also assessed. By correlation analysis, it was concluded that there was no statistically significant relationship between the scores and uptake patterns. On the other hand a compatible increase in the uptake pattern or T/Bg ratio was not observed when the differentiation of the adenocarcinoma raised.

In the current study, when Tl-201 planar and SPECT images were evaluated in 23 cases with prostate cancer, pathological Tl-201 uptakes were observed in the early

Figure 1. *A pathological Tl-201 uptake in the prostatic region is not shown on the early (P: Prostatic region; B: Background) (A), late (B) planar images. It is noteworthy that the increase in activity in the bladder. Transverse SPECT (C) images show a lack of a pathological Tl-201 uptake in the prostatic region Coronal SPECT (D) images show a pathological uptake in the prostatic region.*



planar images in 16/23 patients (69.6%), in the late planar images in 17/23 patients (73.9%) and in the SPECT images in the 20/23 patients (87%). In particular, T/Bg ratios and uptake patterns of the SPECT images were stronger.

The sensitivity and specificity rates for SPECT imaging were calculated as 95.7%, and 77.8%, respectively.

The credibility of the results may be increased by direct anatomic correlation technics, like SPECT/CT. A limitation of this study is interference of the activity in bladder and prostatic urethra with the imaging of the lesion in the prostate gland.

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